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REVIEW ARTICLE

Surgical approach to microwave and radiofrequency liver ablation for hepatocellular carcinoma and colorectal liver metastases less than 5 cm: a systematic review and meta-analysis

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Abstract

Background Primary hepatocellular carcinoma (HCC) and colorectal liver metastases (CRLM) represent the two most common malignant neoplasms of the liver. The objective of this study was to assess outcomes of surgical approaches to liver ablation comparing laparoscopic versus percutaneous microwave ablation (MWA), and MWA versus radiofrequency ablation (RFA) in patients with HCC or CRLM lesions smaller than 5 cm.

Methods A systematic review was conducted across seven databases, including PubMed, Embase, and Cochrane, to identify all comparative studies between 1937 and 2021. Two independent reviewers screened for eligibility, extracted data for selected studies, and assessed study bias using the modified Newcastle Ottawa Scale. Random effects meta-analyses were subsequently performed on all available comparative data.

Results From 1066 records screened, 11 studies were deemed relevant to the study and warranted inclusion. Eight of the 11 studies were at high or uncertain risk for bias. Our meta-analyses of two studies revealed that laparoscopic MW ablation had significantly higher complication rates compared to a percutaneous approach (risk ratio = 4.66; 95% confidence interval = [1.23, 17.22]), but otherwise similar incomplete ablation rates, local recurrence, and oncologic outcomes. The remaining nine studies demonstrated similar efficacy of MWA and RFA, as measured by incomplete ablation, complication rates, local/regional recurrence, and oncologic outcomes, for both HCC and CRLM lesions less than 5 cm ($p > 0.05$ for all outcomes). There was no statistical subgroup interaction in the analysis of tumors < 3 cm.

Conclusion The available comparative evidence regarding both laparoscopic versus percutaneous MWA and MWA versus RFA is limited, evident by the few studies that suffer from high/uncertain risk of bias. Additional high-quality randomized trials or statistically matched cohort studies with sufficient granularity of patient variables, institutional experience, and physician specialty/training will be useful in informing clinical decision making for the ablative treatment of HCC or CRLM.

Keywords Microwave ablation · Percutaneous · Laparoscopic · Radiofrequency ablation · Hepatocellular carcinoma · Colorectal liver metastases

Hepatectomy remains the gold standard treatment for the two most common malignant neoplasms of the liver, primary hepatocellular carcinoma (HCC) and colorectal liver metastases (CRLM) [1–3]. Unfortunately, when considering both contraindications to surgical treatment (e.g., insufficient future liver remnant, tumor size, number, anatomic distribution) and comorbid conditions that increase surgical morbidity, less than 5–20% of patients are suitable candidates for resection [2–6]. Furthermore, the improvement in long-term prognosis has been modest: the 5-year survival rate is estimated at 20–40% [2, 3]. This is especially concerning given the increasing incidence of primary HCC since the 1990s [7]

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and the fact that 25–50% of patients with colorectal cancer will develop CRLM [8–10].

The development of (minimally invasive) techniques for tumor ablation by direct application of chemicals or energy have addressed some of these shortcomings, especially for lesions that are less than 5 cm [2, 11–14]. With the reduced morbidity and mortality compared to resection, these techniques have expanded the pool of eligible patients, can be used to treat small tumor sizes/multiple tumors, and if clinically indicated, may be repeated to treat recurring tumors [13]. Thermal modalities, including radiofrequency (RFA) and microwave (MWA) ablation, represent the most widely-used ablative techniques. RFA treatment is the most common [12] and an accepted approach in selected patients (e.g., HCC lesions smaller than 3 cm) [12, 13, 15]. In contrast, MWA, a more recent addition initially developed for lung cancers [13], has some theoretical benefits over RFA (including less peri-procedural pain, and more predictable ablation) [11–14].

Although both RFA and MWA result in coagulative necrosis via direct application of heat, the physical principles employed are distinct [4, 11–13]. RFA creates a zone of coagulation necrosis through both resistive heating derived from an alternating current driven from the applicator probe (cathode), as well as an accompanying thermal diffusion into adjacent tissues [4, 11]. Comparatively, MWA uses dielectric (electromagnetic) hysteresis which can penetrate tissue that are generally recognized as poor electrical conduits and is generally less reliant on conduction down the thermal gradient (i.e., less indirect application of heat) [11]. MWA can generate more power to produce larger and higher ablation temperatures, but at an increased risk of other complications not as commonly associated with RFA (e.g., thrombosis of the portal vein in cirrhotic patients). Despite our understanding of these physical principles and several systematic reviews on these ablative techniques [2–4, 16], it is unclear how the two modalities and technical variations thereof (laparoscopic, percutaneous, open) compare with respect to procedural-specific morbidity, local/regional recurrence, and survival.

To explore the comparative effectiveness of microwave and radiofrequency ablation, as well as to assess the benefit of percutaneous versus laparoscopic microwave ablation, we conducted a systematic review and meta-analysis to inform our combined society of american gastrointestinal and endoscopic surgeons (SAGES) and americas hepato-pancreato-biliary association (AHPBA) guidelines and ultimately help clinicians in selecting ablative treatment modalities for individuals afflicted with primary or secondary liver neoplasms. Importantly, this systematic review does not compare resection versus ablation and thus should not be interpreted as an endorsement for the use of ablation in respectable lesions (especially for CRCLM and HCC lesions greater than 2 cm). The intent of this systematic review is to document the data available to date of this technology as it is being used more in clinical practice for these tumors.

Methods and materials

To compare the two aforementioned modalities, the SAGES guidelines committee and representatives from AHPBA formed a working group to perform a systematic review and meta-analysis reported here according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17]. Further, due to the few reasonable studies available, the working subgroup decided that procedure specific and short-term outcomes were the primary goal and thus, HCC and CRCLM are grouped together. (The limitation of this combination is discussed in the *Limitations* section further below.) The subgroup originally drafted six questions according to the PICO format (Population, Intervention, Comparator, and Outcomes) to guide the literature search (see Appendix 1 – Note 1). However, on completion of the literature search, the working group realized that only sufficient evidence existed to answer two modified questions as follows:

Key question 1 (KQ1): Should Percutaneous vs. Laparoscopic MW ablation be used for HCC and/or CRLM less than 5 cm?

Outcomes: Incomplete Ablation, Local/Regional Recurrence, Complications, Disease Free Survival (DFS), Overall Survival (OS)

Key question 2 (KQ2): Should MW ablation (laparoscopic or open) vs. RF ablation (laparoscopic or open) be used for HCC or CRLM less than 5 cm?

Subgroup analysis: HCC or CRLM less than 3 cm.

Outcomes: Incomplete Ablation, Local/Regional Recurrence, Complications, DFS, OS

Types of interventions

As described above, all studies comparing percutaneous versus laparoscopic MWA of HCC or CRLM were included, as were any comparative studies of surgical approaches to MWA and RFA (including laparoscopic or open) for the same tumors. Studies that included combined chemoembolization and ablation were also included but tagged for possible source of heterogeneity. Any studies that combined resection with ablation were excluded from our meta-analysis.

Types of outcomes

Five classes of outcomes of interest were specified a priori: (i) incomplete ablation, defined as the number of tumors incompletely ablated out of the total number of tumors (not individual patients); (ii) perioperative complications of Clavien–Dindo grade ≥ 3; (iii) local/regional recurrence, defined as radiologic and/or histologic identification of recurrent tumor at original site or draining lymph nodes after completed ablation; (iv) disease-free survival; and (v) overall survival.

Literature search & eligibility criteria

A clinically guided search was performed for each of the six key questions (Appendix 1 – Note 1) in December 2019, with the assistance of a medical librarian, across seven databases: the Cochrane library, Clinicaltrials.gov, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, PubMed, the WHO's International Clinical Trials Registry Platform (ICTRP), and Google Scholar. The full search criteria and the number of records contributed from each database is provided in Appendix 1 – Note 2, including all publications between 1937 and 2021. All records were combined with EndNote (Clarivate Analytics) then uploaded to Covidence for screening, with duplicates automatically removed in both EndNote and Covidence prior to screening. Exclusion criteria included: reviews that are not systematic reviews and/or meta-analyses, non-English abstracts, non-comparative studies (e.g., case series), and total sample sizes of less than 10 patients across all arms (e.g., case reports or limited case series). An updated search was performed in June 2021 to capture more recent studies or studies not included in the original search.

Study selection

All reviewers participating in the systematic review had received prior training in systematic review methodology. To calibrate reviewers' ratings for study selection and screening, 100 randomly selected abstracts were reviewed by all reviewers on Abstrackr (Brown University, Providence, Rhode Island). All disagreements were discussed during a conference call. Subsequently, all titles and abstracts were screened by two independent reviewers for relevance and eligibility using Covidence. All irrelevant publications were excluded, as were any remaining duplicates or non-English language studies that bypassed our search filters. Full text review by two independent reviewers was subsequently performed. Exclusion criteria included non-comparative studies, case reports, letters to the editors, abstracts, author replies, and lay press articles Only peer-reviewed English language manuscripts meeting screening criteria were included in our final data extraction. It is also important to note that, while reviews were excluded from the pooled analyses, the reference lists were hand-searched for additional relevant references. Discrepancies were resolved through discussion among the reviewers, with a final decision made by the senior author (E.C.) when necessary.

Risk of bias in individual studies

The modified Newcastle–Ottawa Scale was used to assess risk of bias for observational studies(Appendix 1 – Note 3) [18]. Each study was scored by two independent reviewers. Criteria were assessed for risk of bias across three broad categories: selection, comparability, and outcomes. Our minimum length of follow up to be considered 'low risk of bias' from outcomes was a priori defined as 1 year, with length of follow up 3 years or greater as ideal. No randomized control trials were selected for full data extraction, and thus, the Cochrane Risk of Bias Tool was not employed in this systematic review.

Data extraction

Two reviewers independently completed the data extraction forms on Covidence to extract study characteristics, sponsorship source, methods, population (including baseline characteristics), interventions, and a priori determined outcomes. Our primary outcomes, as described above in detail, were incomplete ablation, local/regional recurrence, complication rates, disease-free survival, and overall survival.

Data synthesis

Study data were synthesized quantitatively. We used RevMan (version 5.4 Nordic Cochrane Centre, Copenhagen, Denmark) for meta-analyses. As all relevant data were dichotomous, we estimated risk ratios (RR) with a Mantel–Haenszel (MH) random effects model. Heterogeneity between studies was assessed using I^2 and χ^2 measures. A $p < 0.05$ was considered significant for χ^2 values; a $I^2 < 40\%$ was considered low. We meta-analyzed data when heterogeneity across studies was low or remained unexplained.

Results

Across the bibliographic databases and the 33 records identified through hand searching of systematic review reference lists, total 1066 unique records were screened for eligibility with 11 records deemed relevant to the two review questions (PRIMSA flow diagram Fig. 1). Each record represented a unique study. All 11 studies were of observational design (see Tables 1 and 2).

Key question 1 (KQ1)

Should percutaneous vs. laparoscopic MW ablation be used for HCC and/or CRLM less than 5 cm?

A total of two observational studies, with 81 and 91 patients who underwent liver-directed microwave thermal ablations, met inclusion criteria for KQ1[19, 20]. Unfortunately, both studies were deemed to have a high risk of bias for all outcomes, driven primarily by poor comparability between intervention groups and inadequately defined follow-up periods (Table 3).

Incomplete ablation

Both studies were included in the meta-analysis for incomplete ablation. Data from 54 laparoscopic and 97 percutaneous MW ablations demonstrated a lower risk of incomplete ablation after the laparoscopic approach, although this was not statistically significant (RR 0.28, 95% CI 0.05–1.55, I^2 0%, Fig. 2).

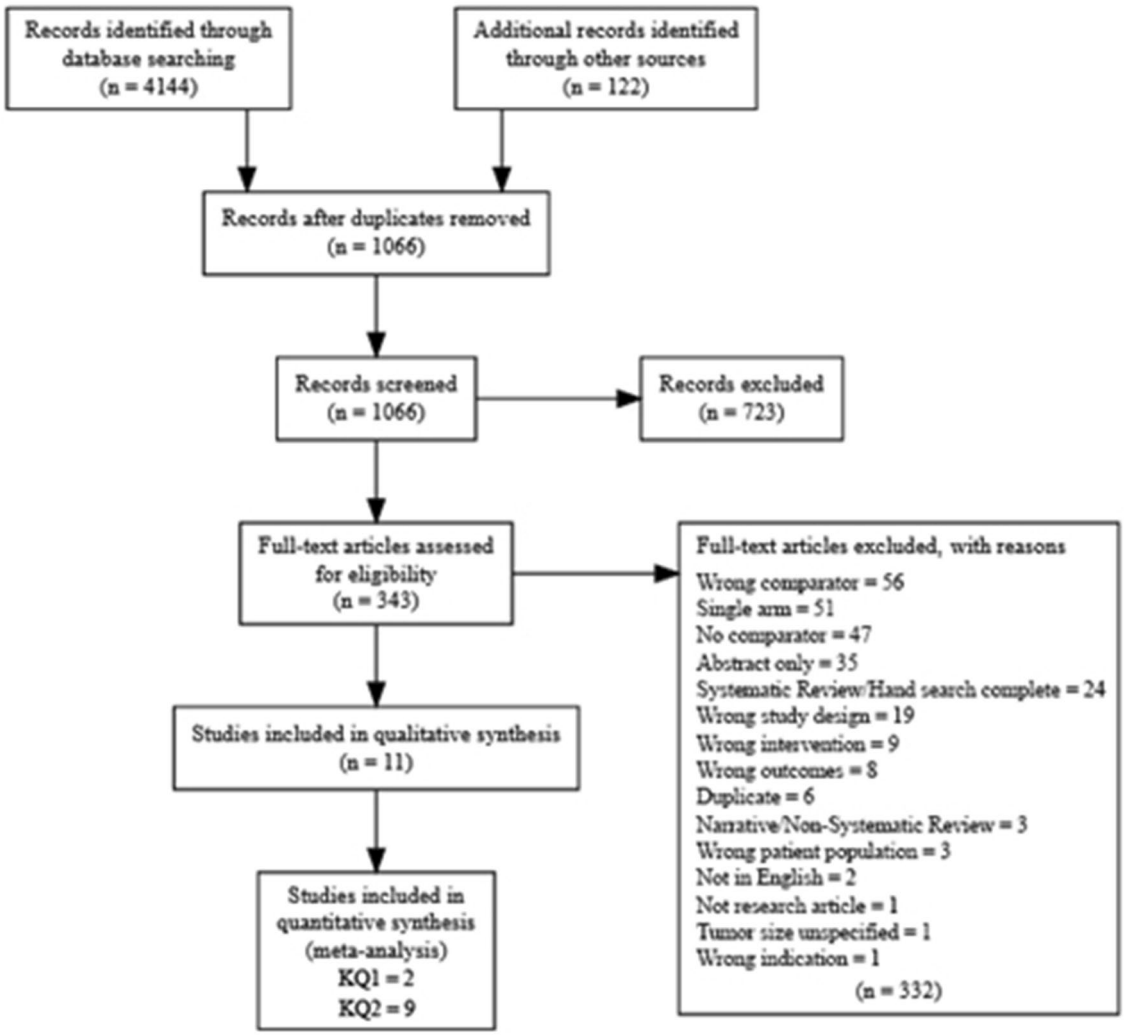

Fig. 1 PRISMA flow diagram for the systematic review. The breakdown by question is summarized in Tables 1 and 2

Table 1 Baseline characteristics of the two studies included to answer KQ1 (percutaneous versus laparoscopic MW ablation)

Study identifier	Intervention	Size	Location	Age	Female/total	Follow-up in months (SD), $N=X$
DeCobelli 2017	Percutaneous MWA	≤3 cm	Distinguished between peripheral (sub-capsular) vs central (intra-parenchymal)	Not reported	Not reported/30	Not reported
	Laparoscopic MWA			Not reported	Not reported/12	Not reported
DellaCorte 2020	Percutaneous MWA	≤5 cm	No	Not reported	17/63	8.9 (11.3), $n=54$
	Laparoscopic MWA			Not reported	6/28	16.8 (9.5), $n=21$

Both studies are retrospective cohort studies from Italian groups that did not have any sponsors listed. No patient from either study underwent embolization. DeCobelli 2017 included both HCC and CRLM, as well as liver metastases from neuroendocrine tumors, pancreatic cancer, lung cancer, and urothelial cancer. DellaCorte 2020 included only HCC patients

MWA Microwave ablation

Criteria For DeCobelli 2017: Inclusion criteria for primary liver tumors included the presence of a potentially curable liver-confined disease, disease unsuitable to hepatic resection alone due to inadequate functional liver reserve, according to EASL–EORTC guidelines. Inclusion criteria for liver metastases included curative intent of liver-confined disease, contraindication to surgery, and local liver disease control when other treatments such as radiotherapy or chemotherapy were applied to an extrahepatic tumor site. Exclusion criteria were pregnancy, the presence of refractory ascites or coagulopathies not susceptible of medical correction. For DellaCorte 2020: Inclusion criteria included clinical and imaging evidence of HCC (radiological diagnosis of tumors on pre-operative dynamic contrast-enhanced CT or MRI with a liver-specific acquisition protocol); disease stage 0, A, B deemed amenable of curative treatment (ablation alone or ablation combined with surgery); ablation within one month of last imaging. ***Group differences*** For DeCobelli 2017: Even though no comparative analysis was done for the groups of interest (percutaneous ablation vs laparoscopic ablation) to check for any group differences, the authors mention that to verify possible confounding effects, a multivariate constrained mixed effect model of the AZ volume as a function of liver condition and operative approach was fitted. The other independent variables considered in this study (sex, age, proximity to capsule and vessels) showed no evidence of improvement when added to the model. For DellaCorte 2020: Compared to LMWA, PWMA had more patients who had previous HCC treatment, less patients treated under general anesthesia, more patients with chronic hepatitis C and less with "idiopathic" as the cause of cirrhosis, more patients with BCLC stage A1 and fewer patients with stage A4 or multifocal disease. A higher amount of energy over tumor size was delivered in laparoscopic ablation. All these group differences were statistically significant ($p<0.05$)

Complications

While neither study was independently significant, meta-analysis revealed an increased MH risk ratio for complications in laparoscopic, versus percutaneous, microwave ablation (risk ratio [RR] = 4.66; 95% confidence interval [CI] = [1.23, 17.22]; Fig. 3).

Local/regional recurrence; 1-year disease-free survival; 1-year overall survival

Only one of the two studies merited inclusion in meta-analyses for the three aforementioned outcomes (DellaCorte 2020). Local/regional recurrence was not non-significant in comparisons of laparoscopic versus percutaneous MWA (RR 0.43, 95% CI 0.10–1.75). Our limitation to outcomes at 1 year was dictated exclusively by the availability of data (i.e., no outcome data beyond 1 year) and were also not significant, with a risk ratio of 1.14 (0.19–1.38) and 1.00 (0.93–1.07), for disease-free and overall survival, respectively.

Key question 2 (KQ2)

Should MW ablation (laparoscopic or open) vs. RF ablation (laparoscopic or open) be used for HCC or CRLM less than 5 cm?

Nine comparative studies met inclusion criteria for KQ2 [21–29]. Six of the nine total studies were deemed to have high or uncertain risk of bias (Table 4). The study cohorts ranged from 35 to 391 patients (Table 2).

Incomplete ablation

Six of nine studies, with data from 348 MWA and 367 RFA, were included in the combined less than 5 cm meta-analysis and revealed no difference between MWA and RFA (RR 1.0, 95% CI 0.05–1.55, I^2 0%, Fig. 4). While the subgroup analysis for tumor less than 3 cm favored MWA, it included one study and was not significant (RR 0.19, 95% CI 0.01–3.88, Fig. 4).

Table 2 Baseline characteristics of the 9 studies included to answer KQ2 (Surgical MWA vs. Surgical RFA). No sponsors or funding sources were reported for any of the studies

Study Identifier	Modality	Size	Country	Cohort	Tumor	Age Mean (SD), $N=X$	Female/total	Follow-up in months Mean (SD), $N=X$
An 2021	MWA	≤3 cm	China	Retrospective	HCC	56.4 (11.5) $N=74$	13/74	Median 37.6 (Range 3.2–79.2)
	RFA					57.4 (10.1) $N=70$	6/70	Median 38.9 (Range 3.4–83.9)
Correa-Gallego 2014	MWA	≤5 cm	USA	Retrospective	CRLM	Median 55 (IQR 48–64), $n=67$	Not reported	Median 18 [95% CI 17–20]
	RFA					Median 56 (IQR 48–65), $n=67$	Not reported	Median 31 [95% CI 28–35]
Lee 2017*	MWA	≤5 cm	China	Prospective	HCC	Median 62.5 (Range 49–79), $n=26$	7/26	47.5 (11.3–62.5)
	RFA					Median 58 (Range 43–77), $n=47$	7/47	52.9 (3.6–121.8)
Sakaguchi 2009	MWA	≤5 cm	Japan	Retrospective	HCC	64.9 (7.8), $N=142$	35/142	Not reported
	RFA					65.6 (8.9), $N=249$	80/249	Not reported
Takahashi 2018	MWA	≤3 cm	USA	Retrospective	CRLM	Not reported	18/51	17 (11–20)
	RFA					Not reported	21/54	18 (12–25)
Yang 2017	MWA	≤5 cm	China	Retrospective	CRLM	Median 51 (Range 39–71) $n=71$	22/71	Not reported
	RFA					Median 50 (Range 42–72) $n=108$	Not reported	Not reported
Iida 2013	MWA	≤3 cm	Japan	Retrospective	HCC	70.1 (6.6), $N=40$	Not reported	Not reported
	RFA					73.5 (4.0) $N=18$	Not reported	Not reported
Simo 2011	MWA	≤5 cm	USA	Retrospective	HCC	59.63 (6.75), $n=13$	6/13	Mean 7 (range 2.5–10.5)
	RFA					58 (8.64), $n=22$	3/22	Mean 19 (range 1.5–31)
Santambrogio 2017	MWA	≤5 cm	Italy	Retrospective	HCC	70 ± 8.3, $n=60$	17/60	31 (19.5)
	RFA					69 ± 9.0, $n=94$	25/94	31 (19.5)

CRLM Colorectal metastases, *HCC* hepatocellular carcinoma, *MWA* microwave ablation, *RFA* radiofrequency ablation, *SD* standard deviation

In Lee 2017: Two patients received TACE as treatment for residual disease. Inclusion and exclusion criteria for each study, as well as a brief discussion of group differences between interventions and tumor locations, is available in Appendix 1 – Note 4

Table 3 Risk of bias for the observational studies included under KQ1 as assessed by a modified Newcastle Ottawa Scale (Color figure online)

Study Id	Final risk of bias	ROB from selection	ROB from comparability	ROB from outcomes
DeCobelli 2017	High	Low	Unclear	High
DellaCorte 2020	High	Low	High	Unclear

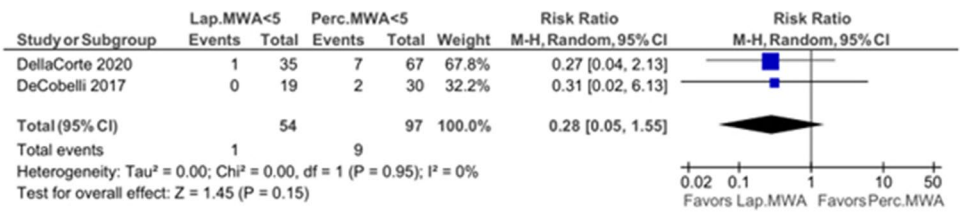

Fig. 2 Forest plot for incomplete ablation with percutaneous MWA as the reference class

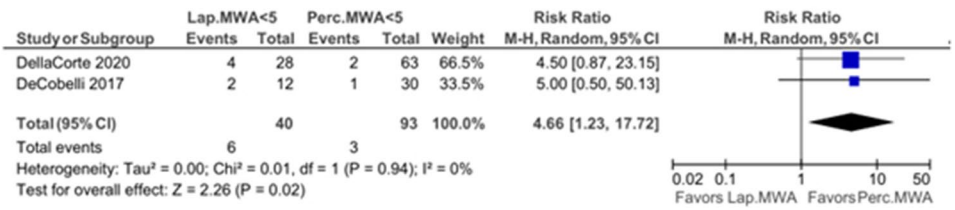

Fig. 3 Forest plot for complication rates of laparoscopic versus percutaneous MW ablation

Table 4 Risk of bias for the observational studies included under KQ2 (MWA vs RFA for lesions smaller than 5 cm), as assessed by a modified version of the Newcastle Ottawa Scale (Color figure online)

Study Id	Final risk of bias	ROB from selection	ROB from comparability	ROB from outcomes
An 2021	Low	Low	Low	Low
Correa-Gallego 2014	Low	Low	Low	Low
Lee 2017	Unclear	Low	Low	Unclear
Sakaguchi 2009	High	High	High	Low
Takahashi 2018	Low	Low	Low	Low
Yang 2017	High	Low	High	High
Iida 2012	Unclear	Low	Unclear	Unclear
Simo 2011	Unclear	Low	Low	Unclear
Santambrogio 2017	High	High	Unclear	Unclear

Complications

Similarly, eight of nine studies, with data from 402 MWA and 480 RFA, were included in the combined less than 5 cm meta-analysis and revealed no difference between MWA and RFA (RR 1.0, 95% CI 0.05–1.55, I^2 0%, Fig. 5). This was consistent for all subgroup analyses, including tumors less than 3 cm (RR 0.78, 95% CI 0.72–1.33, I^2 0%, Fig. 5).

Local/regional recurrence; disease-free survival; overall survival

All comparative meta-analyses between MWA and RFA were non-significant for the three aforementioned outcomes explored in both the cumulative (< 5 cm) and sub-group (< 3 cm) analyses (Figs. 6–8). That is, there were no significant differences between patients who underwent MWA versus RFA with regards to local/regional recurrence (combined MH RR = 0.97, 95% CI 0.73–1.30, $I^2 = 0\%$; Fig. 6). There were also no significant differences for disease-free survival at 1 year (combined MH RR = 0.99, 95% CI = 0.83–1.19, $I^2 = 15\%$), 3 years (RR = 1.03, 95% CI = 0.73–1.45, $I^2 = 0\%$), and 5 years (RR = 1.09, 95% CI = 0.79–1.51, $I^2 = 0\%$; Fig. 7). Similarly, we observed no significant differences in the meta-analyses for overall survival at 1 year (RR = 0.99, 95% CI = 0.97–1.01, $I^2 = 7\%$), 3 years (RR = 0.99, 95% CI = 0.94–1.05, $I^2 = 0\%$), and 5 years (RR = 1.01, 95% CI = 0.91–1.11, $I^2 = 0\%$; Fig. 8).

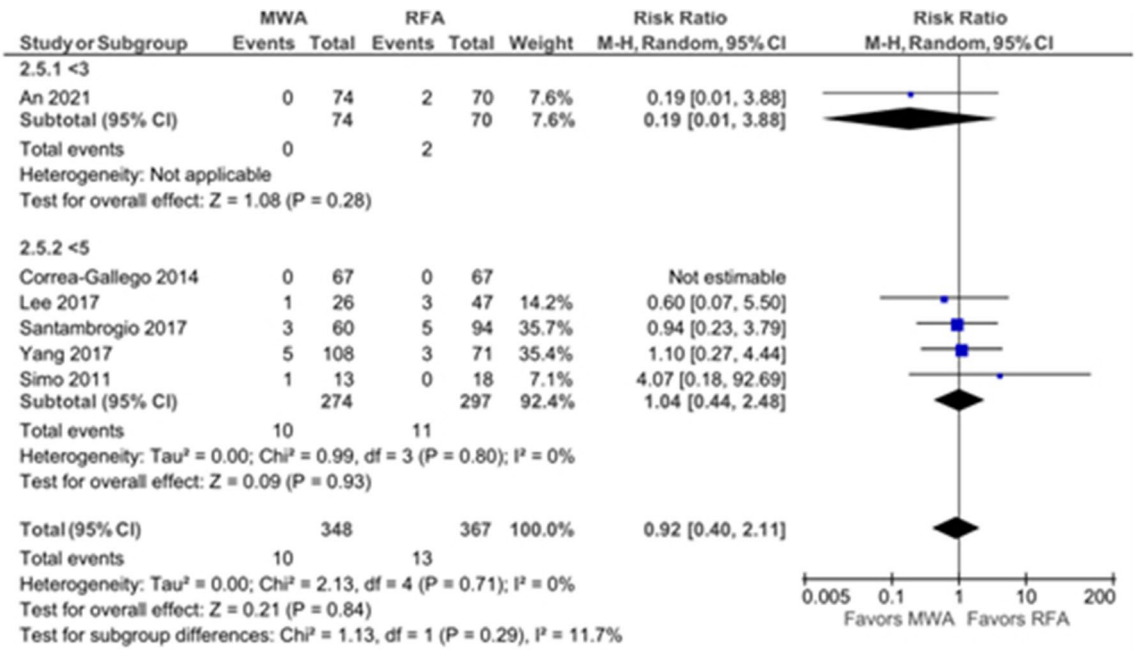

Fig. 4 Forest plot for incomplete ablation with RFA as the reference class

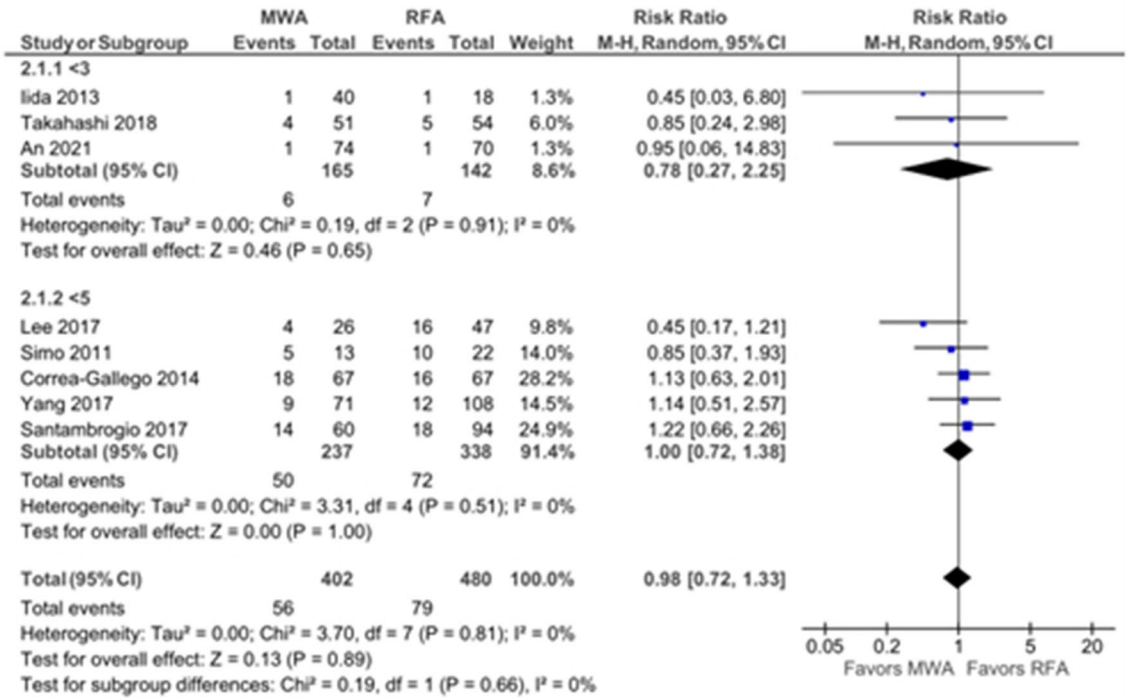

Fig. 5 Forest plot for complication rates with RFA as the reference class

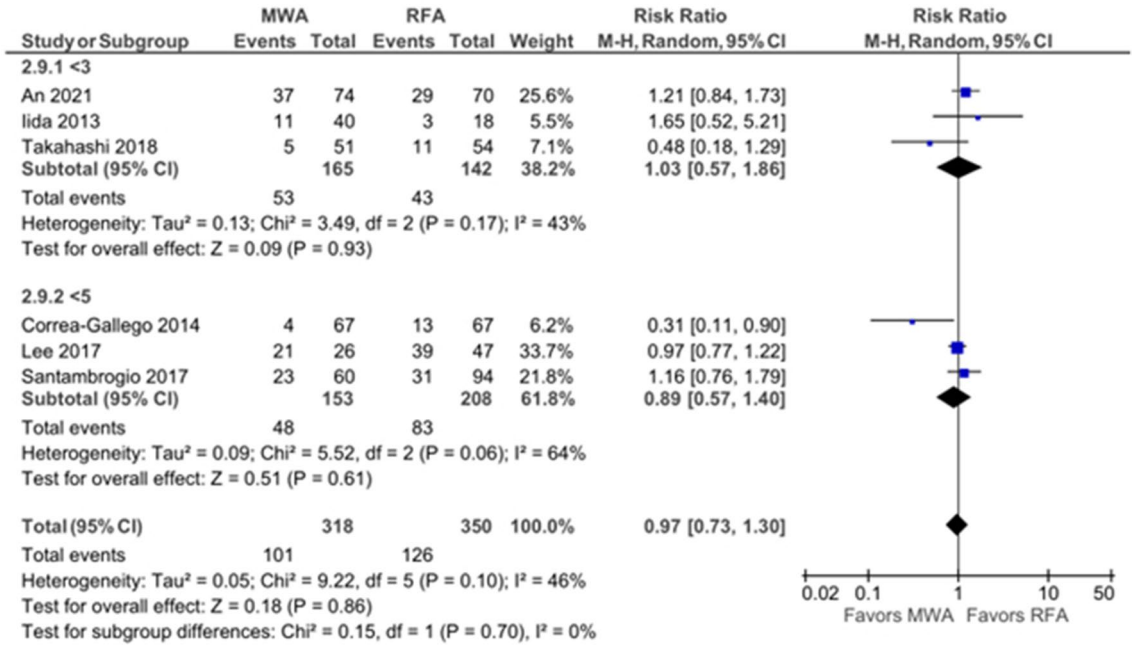

Fig. 6 Forest plot for local/regional recurrence with RFA as the reference class

Discussion

The purpose of this systematic review was to review the literature and pool appropriate comparative data to better inform clinical decision making regarding both the ablative modality and technical approach for the treatment of the two most common malignant liver neoplasms. Critically, this systematic review is not a comparison of resection versus ablation.

Despite a comprehensive literature search, we identified less than a dozen relevant studies with the majority at high or uncertain risk of bias. Within these constraints, we noted that the efficacy of MWA, as measured by incomplete ablation, complication rates, local/regional recurrence, and survival, appears similar to that of RFA both for HCC and CRLM lesions less than 5 cm. This was consistent in the subgroup analysis of lesions less than 3 cm. With regards to approach, laparoscopic MWA had significantly higher complication rates, but otherwise similar risk of incomplete ablation, local/regional recurrence, and survival.

These results are not an endorsement of the of ablation in respectable lesions, especially for CRCLM and HCC > 2 cm. Ablative technology is just one component of the treatment algorithms, which include surgery, chemotherapy, radiation therapy, as well as liver-directed therapies (none of which are explored or investigated in this systematic review).

Relationship to literature

There have been several comparative studies [30–32] and systematic reviews [33–35] that have attempted to address outcomes (including local disease control and survival) of percutaneous MWA versus RFA for HCC and CRLM. While most of these studies hint at similar completion frequencies, complication rates, and survival between MWA and RFA, they disagree with regards to local tumor control and progression [33, 34]. This controversy, in part, stems from substantial variation in the clinical contexts in which these ablation technologies were deployed (e.g., tumor size, number, anatomic distribution, as well as patient profiles/comorbidities), making it difficult to compare or to perform a meta-analysis of the results. Further, none of these studies have explored other surgical approaches (e.g., laparoscopic, or open). Our analyses here suggest that laparoscopic or open MWA and RFA are similarly safe and effective for lesions smaller than 5 cm. However, given the limited evidence and quality, these results are not definitive. In contrast, very few studies have compared percutaneous and laparoscopic MWA of malignant liver neoplasms [19, 20]. Thus, while this limits the power of our meta-analysis, our systematic review provides a comprehensive look at the existing literature. Our results suggest that percutaneous MWA is safer than laparoscopic MWA, with regards to complication rates, but no difference in ablative completeness rates or survival. Although given the major differences in patients included in each cohort (including more multifocal disease patients

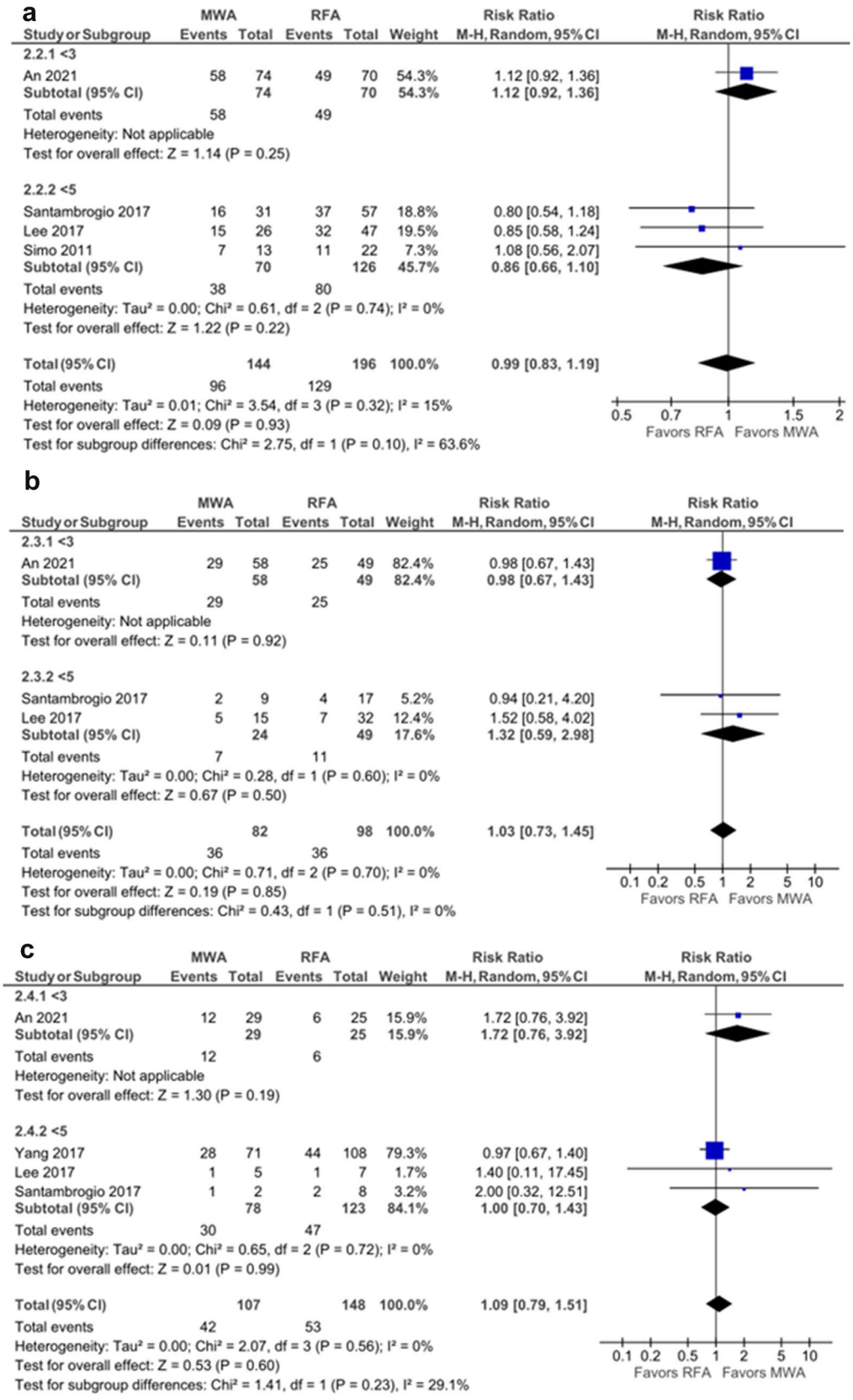

Fig. 7 Forest plot for DFS with RFA as the reference class at: **a** 1 year; **b** 3 years; and **c** 5 years

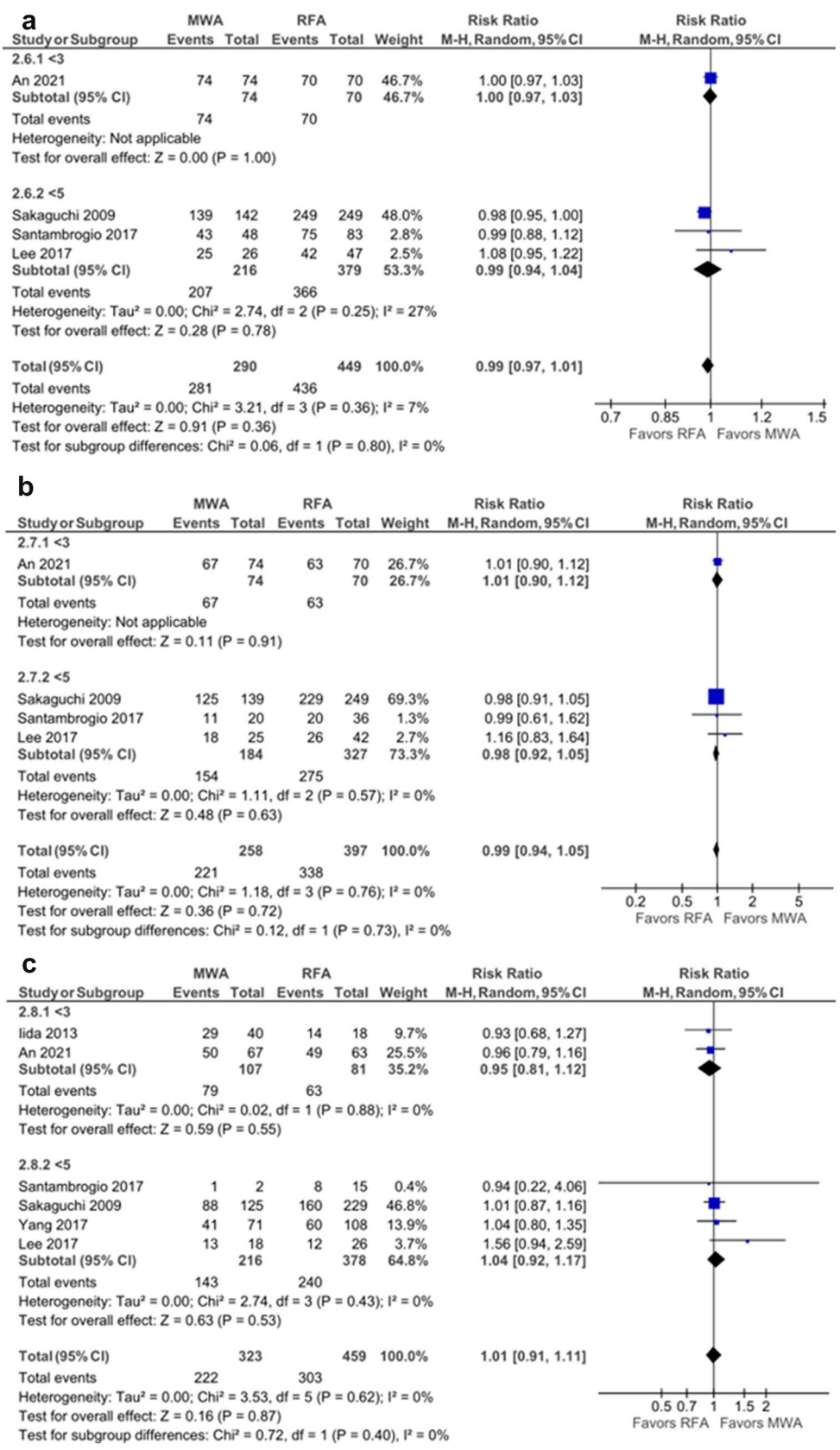

Fig. 8 Forest plot for OS with RFA as the reference class at: **a** 1 year; **b** 3 years; and **c** 5 years

in the laparoscopic group, as well as overall sicker patients with higher incidence of chronic hepatitis C), it is unclear how confounded these observations are.

Limitations

All 11 comparative studies included in our analyses were observational (all but one being retrospective cohort studies), with relatively small sample sizes and short follow-up. Furthermore, the majority (two out of two of the percutaneous versus laparoscopic MWA studies, and five of nine of the MWA vs RFA studies) were deemed at either uncertain or high risk of bias. No randomized clinical trials met our inclusion criteria. Altogether, the paucity of high-quality evidence limits the definitive with which we can present these conclusions. Restrictions in our literature search (e.g., to English language only studies) are likely to have had minimal impact, given both the national/geographic diversity of the included studies (China, Egypt, Italy, Japan, and USA) and that only two full text articles were excluded (Fig. 1).

It is also important to note that HCC and CRCLM are distinct diseases when looking at treatment algorithms and overall survival. The goal of this systematic review was to assess what data are available on differences between MWA and RFA rather than to make any argument that ablation is superior to resection or any other therapy. In fact, we think it is inappropriate to make any such claim with the current available evidence. A surgeon or multi-disciplinary group should always make the decision when ablation is appropriate. Due to the lack in number of reasonable studies to include in such a review of what is currently an important question considering the rapid adoption of MWA of the last several years with very little data, the working group decided that procedure specific and short-term outcomes were the primary goal. Thus, we included HCC and CRCLM as one analysis.

Relevance to clinical practice

Our findings suggest MWA and RFA for HCC or CRLM lesions less than 5 cm are comparable with respect to efficacy and safety. Further, our results also support that percutaneous MWA should be preferred to laparoscopic approaches due to lower complication rates. However, as discussed above, given the limited evidence and quality of data, these results do not definitively eliminate the clinical equipoise surrounding our PICO questions.

Future research recommendations

Given the paucity of comparative observational studies and the complete absence of randomized control trials, there is a pressing need for higher-quality evidence to inform both selection of the ablative technology and technical approach. This evidence must have adequately sufficient follow-up and must clearly define the clinical contexts/indications (if any) in which one approach or technique may be preferred over another (e.g., tumor size or anatomic distribution). We encourage researchers to ensure sufficient granularity in the data (e.g., molecular biology, location, experience of institution, and physician specialty [e.g., interventional radiology vs surgery]) to help discriminate between institutional and intervention effects, as well as identify appropriate patients for each intervention.

Conclusion

Available evidence indicates that there was no difference between MWA and RFA treatment with a surgical (laparoscopic or open) approach for HCC or CRLM lesions less than 5 cm, with respect to safety or efficacy. Further, percutaneous MWA is preferable to laparoscopic approaches due to lower complication rates but is otherwise comparable with respect to completeness rates and survival.

Placing this systematic review in the broader clinical context, it is critical to note that ablative technology is only one treatment modality – an increasingly used part of treatment algorithms, which also include liver-directed therapies, surgery, chemotherapy, and radiation. However, this systematic review does not compare, nor endorse ablation in preference to any of these modalities. Ultimately clinicians and multi-disciplinary groups should offer recommendations based on the clinical criteria for each individual patient.

Our systematic review also revealed a definitive need for high quality comparative/population-based studies to better guide clinical decision making. While the evidence is limited and of variable quality, the results described here will form the basis of an upcoming integrated SAGES-AHPBA clinical practice guideline.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00464-022-09815-5.

Declarations

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